UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,091	05/06/2005	Juha-Matti Savola	TUR-168	2654

32954 7590 11/16/2007

JAMES C. LYDON
100 DAINGERFIELD ROAD
SUITE 100
ALEXANDRIA, VA 22314

EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	**PAPER NUMBER**
1614	

MAIL DATE	DELIVERY MODE
11/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,091	SAVOLA ET AL.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *18,21,22 and 30* is/are allowed.

6)☒ Claim(s) *11-17,19,20,23-29,31 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed **6/8/07**presents remarks and arguments to the office action mailed **3/8/07**. Applicant's request for reconsideration of the rejection of claims in the last office action has been considered.

Applicant's arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of Claims

Claims 11-32 are pending and examined in this office action, Claims 23-32 are newly applied. Claims 11, 14 and 19 are currently amended.

Allowable Subject Matter

Claims 18, 21-22 and 30 are allowed.

Maintained Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11,14-17, 19-20, 23 and 26-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims recite substituted imidazole derivative of formula I. However, the "derivatives" of the compounds of Claim 11 are not defined in the instant disclosure. A lack of adequate written description issue arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967).

An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.

A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]."

In other words, the Applicant has not described with sufficient clarity what these derivatives of the substituted imidzole derivatives of formula I are contemplated. The "derivative" of the compounds of Claim 11 is not defined in the specification so as to know the structures of the compounds that are included and/or excluded by the term. Therefore, the specification lacks adequate support for Claims 11-20. Examiner suggest in order to overcome this rejection, to cancel the word derivative from the claim.

Claims 11-13, 14-15, 17 and 18, 26-27 and 29 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The

claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims recite preserving agents.

Applicant argues that these agents are disclosed in the specification and that one of skill in the art would immediately envision what the preservatives are.

It maybe so, but with regard to the compound it would not be clear as to what preservative agent would actually preserve the compound. Therefore written description is appropriate. Simply stating preserving agent (for example) will not apprise the skilled artisan of the type of preserving agent to use. The term preserving agent is very broad, the use of one type of preserving agent might not be appropriate for the compound. Special preserving agents are used for certain formulations and not all preserving agents are suitable.

Applicant's arguments have been fully considered but they are not persuasive.

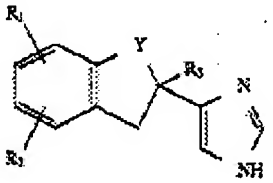
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

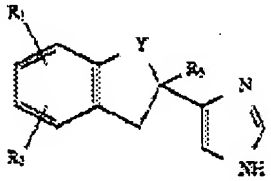
> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 23-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Karjalainen et al. US 5,498,623.

The above reference teaches the claimed compound as in current claim

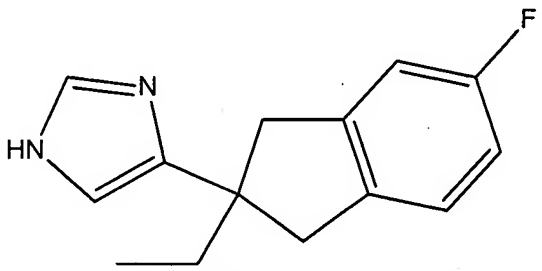


11 which is identical to the claimed compound of the claimed

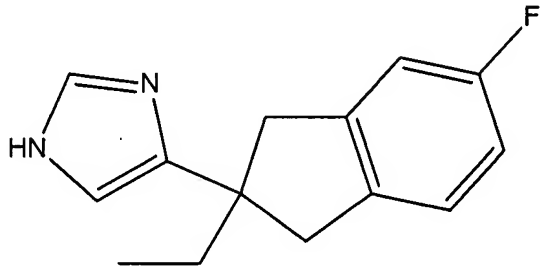


invention , wherein Y is CH_2 or CO, R_1 is a halogen or hydroxyl, R_2 is hydrogen or halogen and R_3 is hydrogen or lower alkyl-methyl (see abstract in a pharmaceutical composition (see abstract also). Administered orally. See col. 4, lines 62-63. Mucosal administration is a moist tissue lining such as the mouth, stomach intestines and respiratory tract. Thus administration of the composition orally is via mucosal.

With regards to claims 24 and 25 the reference teaches (see abstract



also) 4-(2-ethyl-5-fluoro-2,3-dihydro 1H indan-2-yl)-1H-imidazole is the same as



4-(2-ethyl-5-fluoro- indan-2-yl)-1H-imidazole or its salts. As to the hydrochloride salt of the said formula the reference teaches the preparation of such salt (see col. 7, lines 48-50).

Maintained Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11-17, 19-20, 23-29 and 31-32 remain and are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Karjalainen et al. US 5,498,623 taken with Geerts et al et al. US 5,658,938 in view of Chauveaux et al. US 6,326,401 and Huupponen et al. Clinical Pharmacol. Ther 1995;58:506-511 (applicants prior art submission).

Applicant argues that Oral administration of a substituted imidazole derivative conforming to formula (1) has been associated with' compromised cardiac safety and rapid decomposition of the derivative. The applicants have discovered these problems of compromised cardiac safety and rapid decomposition can be avoided by oromucosal administration. Applicant also argues that neither Karjalainen et al. nor Geerts et al et al. disclose an ormucosal formulation. Chauveau et al. merely discloses the utility of capryl caproyl macrogel glycerides in delivering tryptan-like non-polypeptide substances via buccal administration. Finally, Huupponen et al. differs from the claimed invention because atipamezole does not contain a halogen or hydroxyl at R1. Neither halogen or hydroxyl are bioisoteric with the hydrogen in atipamezole. Thus, the subject matter of the claims cannot be considered obvious to one of ordinary skill.

In response, Applicant is arguing what is not set forth in the claims, for example claim 11 recites an oral mucosal formulation, what it does have no patentable weight. As to the allegation that the references cannot be considered obvious is found unpersuasive because the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so

found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the Karjalainen et al. disclose the compound, same as claimed by applicant administered orally. Although the reference did not verbertum teach the formulation as oral mucosal, one of ordinary skill in the art would have known that oromucosal preparations are solid, semi-solid or liquid preparation that are administered via the mouth, therefore teaches the claimed invention. See col. 4, lines 65. Secondly, the reference suggest the addition of other auxillary agents to the formulation such as suitable solvents, colors etc. Where Karjalainen et al. fails, Geerts et al. teach an imidazole compound (see abstract) wherein the composition comprises flavoring-thus interpreted as sweetening agents. One of ordinary skill in the art would have been motivated to add flavoring or preservatives to the formulation as taught by Chauveaux.

Careful consideration has been given to the arguments but found unpersuasive and the rejection is maintained.

The rejection below include newly added claims

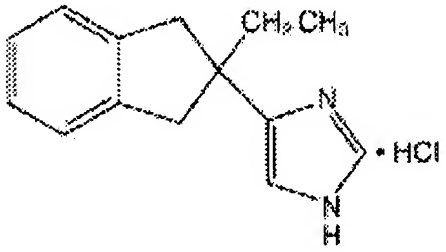
Karjalainen et al. is applied here as above, to instant claims 11-13. The reference also teaches with regard to ethanol as the solvent as required by instant claims 15 and 27. See col. 7, lines 63-64.

The Geerts et al. teach an imidazole compound (see abstract) wherein the composition comprises flavoring-thus interpreted as sweetening agents as in the instant claim 14 and the solvent is water (see col. 11, lines 16-20) as in claims 14-15

and 27. Known flavoring agents are lactose, aspartame glucose etc. One of ordinary skill in the art would have been motivated to use a common flavoring agent and it is within the skill artisan to choose. Thus obvious variation of the types of flavors.

Even though the above references did not teach the addition of a preservative to the composition. However, the Chauveaux et al. teach, the use of methyl and propyl parahydroxyybenzoate in an oramucosal formulation (see col. 3, lines 36-45) as required by instant claims 11, 16, 26 and 28.

Huupponen et al. teach antipamezole hydrochloride (see abstract) a drug that is within the core structure of the claimed compound



, wherein the solvent is water and alcohol-thus mixture thereof is within the claim limitation (see page 506, sec methods under heading and also page 507, under drug administration) as in the instant claim 15, in a form of spray (wherein one to four shots were given from bottles with atomizer designed to deliver...) (see lines 8-10 under drug administration, pg 507) as in claims 19-20 and 31-32. The reference also teaches the drug is oromucosal (see pg, 506, rt. col. four lines from the bottom).

One of ordinary skill in the art would have been motivated to make an oromucosal formulation of the above compound with a preservative because the Chauveaux et al. teach the composition of an oro-mucosal that comprises a

preservative. The addition of the preservative is for preserving the homogenous formulation as taught in col. 3, lines 39-42. Thus one of ordinary skill in the art would have been motivated to incorporate the addition of a preservative in the formulation. Also, the cited references did not teach a particular favoring to the composition, however, one of ordinary skill in the art would have added flavorings to the composition to improve on its taste and especially used black currant because it does not only gives flavor it also adds color that is appealing particular to kids. Thus one of ordinary skill in the art would be motivated to use a flavor that will give both taste and color to the drug that is used for oro-mucosal administration.

Thus, the claimed invention was prima facia obvious to make and use at the time it was made.

Maintained Double Patenting

Claims **11 –17 and 19** remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim **1-3 and 12-18** of U.S. Patent Application No. **10534117.** Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows:

Both sets of claims refer to a formulation – oromucosal formulation of compound of formula I as above in the current application (claims 11 –17 and 19) and fast dispensing solid forms (claims 1-3 and 12-18) in the copending application. The current application claims anticipate the copending application claims

Applicant's request that the Double Patenting rejection be held in abeyance until it is made permanent is noted but will be maintained in this Office Action and future Office Actions until withdrawn. Applicant, have not presented a terminal disclaimer and the

claims of the above co-pending rejection remain pending, since this is not the only or sole rejection remaining the rejection is properly maintained.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SVG
11/05/07

Ardin H. Marschel 11/13/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER